

Letter to the Editor

Lymph Node Lesion of Acute Infectious Mononucleosis in the Elderly : A Case Report

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TO THE EDITOR

We present here lymph node lesion of infectious mononucleosis (IM) in an elderly patient.

An 80-year-old Japanese woman presented with a 1 month history of left supraclavicular lymphadenopathy accompanied by high-grade fever, general fatigue and swelling in the bilateral submandibular gland region. Physical examination on admission demonstrated systemic lymphadenopathy up to 40 mm in diameter. The hemoglobin was 12.0 g/dL, white blood cell count $10.5 \times 10^9/L$ (atypical lymphocytes 25%) (Fig. 1a) and platelet count $205 \times 10^9/L$. Serum protein electrophoresis demonstrated a polyclonal hyper- γ -globulinemia. Measurement of serum immunoglobulin (Ig) levels demonstrated the following: IgG 4,856 mg/dL, IgA 707 mg/dL and IgM 314 mg/dL. Subsequent serologic tests for Epstein-Barr virus (EBV) showed a previous infection pattern: a viral capsid antigen (VCA) IgG titer of 4.5 (< 0.5 mg/dL), a VCA IgM titer of 0.0 (< 0.5 mg/dL), an early antigen (EA) IgG titer of 0.2 (< 0.5 mg/dL), and an EBV nuclear antigen (EBNA) titer of 1.5 (< 0.5 mg/dL). However, abnormal high titer of EBVDNA (7.6×10 ; normal range $< 2.0 \times 10$) was detected in peripheral blood.

Cervical lymph node biopsy was performed. Information from flow cytometry of the biopsied specimens showed a polyclonal B cell population. There was no absence of pan-T-cell markers. The patient treated with prednisolone, and she is currently alive without disease 14 months after disease onset.

Tissue specimens were fixed in formalin solution, routinely processed and embedded in paraffin. For light microscopic examination, the sections were stained with hematoxylin-eosin (HE). Immunohistochemical studies were performed using the antigen retrieval method on the Histofine Histostainer (Nichirei Bioscience Inc, Tokyo, Japan) according to the manufacturer's instructions. The panel of antibodies included, human immunoglobulin light chains (κ and λ), SP7 (CD3), 4C7 (CD5), L26 (CD20), MCS-1 (CD15), and CD30 (1G12) (Nichirei). Sections with known reactivity for antibodies assayed served as positive controls and sections treated with normal rabbit and mouse serum served as negative controls.

In situ hybridization (ISH) with EBV-encoded small RNA (EBER) oligonucleotides was also performed to test for the presence of EBV small RNA in formalin-fixed paraffin-embedded sections using the hybridization kit (Dako A/S, Glostrup, Denmark).

DNA was extracted from paraffin-embedded sections. The variable region (CDR2 and FW3) and VDJ region (CDR3) of immunoglobulin heavy chain (IgH) gene were amplified by semi-nested PCR, using primers of FR2B, LJH and VLJH, according to a previously described method.¹ Primers were as follows: 5'-CCGG (A/G) AA (A/G) (A/G) GTCTGGAGTGG-3', as upstream consensus V region primer (FR2B); 5'-TGAGGAGACGGTGACC-3', as a consensus J region primer (LJH); 5'-GTGACCAGGGT [A/C/G/T] CCTTGCCCCAG-3', as a consensus J region primer (VLJH). PCR products were estimated to be about 200-300 bps in length.

Histologically, on low power field, the biopsied specimens demonstrated numerous lymphoid follicles with normal or atrophic germinal centers and interfollicular widening (Fig. 1b). Marked proliferation of arborizing vessels was noted in the interfollicular area (Fig. 1b). The lymphoid sinuses occasionally appeared to be compressed by the paracortical expansion. The paracortical area and medullary cords were heavily infiltrated with small and medium-sized lymphocytes, mature plasma cells, plasmacytoid cells, immature plasma cells, im-

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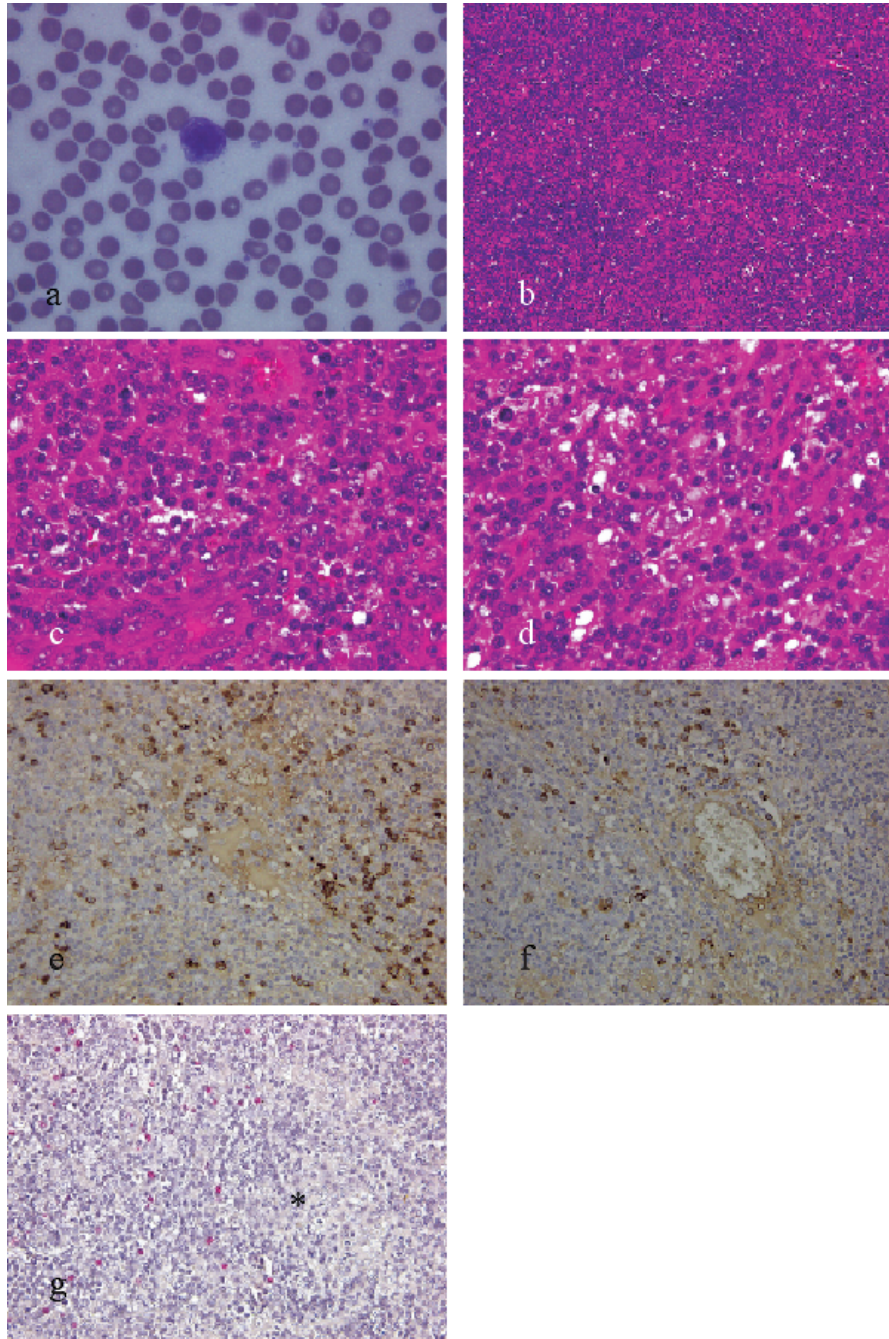


Fig. 1. Histologic and immunohistochemical findings. (*1a*) Note a large immunoblast in the peripheral blood. (Wright's-Giemsa). (*1b*) Lymph node biopsy specimen. On low power field, the biopsied specimens demonstrated lymphoid follicles with normal or atrophic germinal centers and interfollicular widening with marked proliferation of arborizing vessels. (*1c*) On high power field, the paracortical area and medullary cords were heavily infiltrated with small and medium-sized lymphocytes, mature plasma cells, plasmacytoid cells, immature plasma cells, immunoblasts and histiocytes with or without epithelioid cell features. (*1d*) Note an immunoblast that somewhat resembled a Hodgkin cell. (*1e*) The plasma cells, plasmacytoid cells, immature plasma cells and B-immunoblasts showed polytypic intracytoplasmic immunoglobulins. (*1e*) & (*1f*) Immunostaining of κ (*1e*) & λ (*1f*) light chains. (*1g*) *In situ* hybridization of Epstein-Barr virus (EBV)-encoded small RNA oligonucleotide (EBER). Note the numerous EBV-infected lymphocytes in the germinal center (*) as well as in the interfollicular area.

munoblasts and histiocytes with or without epithelioid cell features (Fig. 1c). However, there were no intracytoplasmic pseudoinclusions (Dutcher bodies) observed in the plasma cells. A portion of the immunoblasts somewhat resembled Hodgkin (H) cells (Fig. 1d). The majority of the large transformed lymphocytes including immunoblasts expressed B-cell antigen. Immunohistochemical studies of light chain determinants for interfollicular plasma cells, plasmacytoid cells and B-immunoblasts demonstrated a polyclonal pattern (Figs. 1e & 1f). A portion of the large lymphoid cells including H cells were CD30⁺, but CD15⁻.

There were numerous EBER + large lymphoid cells both in the interfollicular area and in the lymphoid follicles (Fig. 1g).

Genotypic studies demonstrated only germline bands with immunoglobulin heavy-chain probes.

IM is an acute lymphoproliferative disorder that typically occurs in young patients and is usually caused by EBV.² The diagnosis of IM is usually based on clinical and serological findings.^{2,3} However, when IM occurs in elderly individuals, it frequently presents diagnostic problems.^{4,5} Only a few reports detailed clinical, histological and immunohistological findings of IM in elderly have been published in the literature.⁶⁻⁸ The histomorphological findings of IM in elderly patients appear similar to those of typical IM in younger patients.^{7,8} However, clinical presentations of IM in elderly are quite distinct from the clinical findings of IM in younger patients, including absence of atypical lymphocytosis of the peripheral blood.⁶⁻⁸ Indeed, this patient underwent lymph node biopsy to rule out malignant lymphoma. Histologically, the lymph node lesion contained numerous plasma cells, cells with plasma cell differentiation and B-immunoblasts and suspected atypical lymphoproliferative disorder. However, the combination of clinical, immunophenotypic, and genotypic findings indicated that this patient can be regarded as having an essentially benign reactive process. Moreover, the distribution pattern of EBER⁺ cells in this case indicates recent EBV infection (IM pattern) as described by Kurth *et al.*⁹ Systemic polyclonal immunoblastic proliferation (SPIP) is a rare lymphoproliferative disorder.^{10,11} SPIP frequently affects middle-aged and elderly patients. SPIP is characterized by pronounced "B" symptoms and pronounced peripheral blood plasmacytosis and immunoblastosis.^{10,11} Lymph node lesions show diffuse infiltration of immunoblasts and plasma cells.^{10,11} Clinical, laboratory and pathological findings in this patient were similar to those of SPIP. The present case suggests that at least a portion of SPIP appears to be IM related to the reactivation of EBV in middle-aged or elderly populations.¹² Finally, serologic tests for EBV in this case showed a previous infection pattern in an elderly IM patient.

EBV DNA test in the peripheral blood and/or ISH to test for the presence of EBV small RNA in formalin-fixed paraffin-embedded sections are important to confirm the diagnosis.

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